

Attorney Docket No.: KBI-0003
Inventors: Ranganathan and Dickstein
Serial No.: 09/557,011
Filing Date: April 20, 2000
Page 3

I. Rejection of Claims Under 35 U.S.C. §103

The Examiner has rejected claim 1-4 under 35 U.S.C. §103(a) as being unpatentable over Yatzidis et al. (1979) in view of Prakash et al. (1995), and further in view of Goldenhersh et al.

The Examiner suggests that claims 1-4 of the present application are drawn to a microencapsulated formulation comprising a mixture of sorbents and a bacterial source, wherein the sorbents have absorption affinities for substances such as ammonia, urea, creatine, phenols and indoles.

The Examiner suggests that Yatzidis et al. disclose that locust bean gum showed a beneficial effect on patients with renal failure (uremia). Locust bean gum was shown to have the ability to absorb urea, creatine, uric acid, ammonia phosphorus, chloride and sodium. The Examiner acknowledges that Yatzidis et al. do not specifically mention the combination of locust bean gum with a bacterium.

Prakash et al. (1995) is suggested to disclose a method for treating uremia by the use of a microencapsulated *E. coli* strain (DH5). Prakash et al. (1995) is further suggested to teach *E. coli* cells efficiently depleted urea and further indicated that the same bacteria lowered overall ammonia levels.

Attorney Docket No.: KBI-0003
Inventors: Ranganathan and Dickstein
Serial No.: 09/557,011
Filing Date: April 20, 2000
Page 4

Goldenhersh et al (1976) is suggested to teach a need for more effective carbon detoxification. The Examiner suggests that although Goldenhersh et al. and Prakash et al. do not specifically teach both microencapsulation and enteric coating, Goldenhersh et al. do teach microencapsulation with cellulose acetate. The Examiner suggests therefore, that the charcoal composition was microencapsulated as well as enteric coated. Alternatively, the Examiner suggests that it would not have required a substantial inventive contribution from one of ordinary skill in the art to have added an additional coating on an already enterically coated capsule. Applicants respectfully disagree.

To establish a *prima facie* case of obviousness under 35 U.S.C. 103(a) three basic criteria must be met. MPEP § 2143. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art must teach or suggest all of the claim limitations.

Applicants' invention is a microencapsulated and enteric coated composition comprising: a microencapsulated and enteric

Attorney Docket No.: KBI-0003
Inventors: Ranganathan and Dickstein
Serial No.: 09/557,011
Filing Date: April 20, 2000
Page 5

coated mixture of sorbents with specific adsorption affinities for uremic toxins wherein the sorbents comprises oxystarch, locust bean gum, and activated charcoal; and a bacterial source which metabolizes urea and ammonia. The composition has both a microencapsulated coating and an enteric coating. Claim 1 has been amended to clarify that the composition comprises two distinct coatings, for example, that the enteric coating disintegrates and dissolves at or above a PH of 7.5; and further that the bacterial source which metabolizes urea and ammonia is kept within the microencapsulated coating to prevent microbial infection of patients, as supported throughout the specification and at pages 8-9. None of the recited art teaches or suggests such a double coated composition for delivery of sorbents and bacteria.

Further, Yatzidis et al. do not teach a combination of sorbents with any bacterium. There is no teaching of any enteric coating, nor is there any teaching of any microencapsulated coating. Prakash et al. simply teach a microencapsulated *E. coli* source as useful for reducing ammonia levels. There is no teaching of any enteric coating. Finally, Goldenhersh et al. teach a microencapsulated form of charcoal which is further taught to be unsuccessful for significant recovery of uric acid

Attorney Docket No.: KBI-0003
Inventors: Ranganathan and Dickstein
Serial No.: 09/557,011
Filing Date: April 20, 2000
Page 6

capacity, see page 253, column 1. Contrary to the Examiner's suggestion, the composition taught by Goldenherhsh et al. does not contain two coatings as taught by the present invention(i.e. microencapsulated as well as enteric coated). The Goldenherhsh et al. compound has only one coating. As described in the specification and claim 1, the purpose of the microencapsulated coating is to prevent the bacterial source from infecting patients. The cellulose acetate suggested by the Examiner to be an enteric coating does not fall within the definition of an enteric coating (as set forth in the specification at page 8, lines 25-34). The cellulose acetate would not dissolve at a pH of 7.5 or greater to dissolve and deliver the sorbents and microencapsulated bacterial source at the ileal and colonic regions of the bowel, see pages 8-9. Rather, the cellulose acetate taught by Goldenherhsh et al. would be considered to be a microencapsulation polymer, see page 9, lines 8-12.

Further, as the microencapsulated coating was not taught or suggested to be successful by Goldenherhsh et al. it does not follow that one of skill in the art would be motivated to combine an additional coating with the composition, as another coating would not provide any further advantage.

Attorney Docket No.: KBI-0003
Inventors: Ranganathan and Dickstein
Serial No.: 09/557,011
Filing Date: April 20, 2000
Page 7

The recited art fails to teach all of the limitations of claim 1. None of the recited art teach an enteric coated and microencapsulated composition as recited in claim 1. Thus, the references fail to establish a *prima facie* case of obviousness against the pending claims 1-4. Accordingly, this combination of references does not teach or suggest the present invention.

Withdrawal of this rejection is respectfully requested.

MPEP § 2143 and the Courts are quite clear; both the teaching or suggestion to make the claimed combination and the reasonable expectation of success must be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). The cited combination of prior art fails to provide this reasonable expectation of success. It is only with the instant specification in hand, which demonstrates the efficacy of Applicants' invention that one of skill has a reasonable expectation of success.

Withdrawal of this rejection is therefore respectfully requested.

Attorney Docket No.: KBI-0003
Inventors: Ranganathan and Dickstein
Serial No.: 09/557,011
Filing Date: April 20, 2000
Page 8

II. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "Version with Markings to Show Changes Made".

Respectfully submitted,

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Attorney Docket No.: KBI-0003
Inventors: Ranganathan and Dickstein
Serial No.: 09/557,011
Filing Date: April 20, 2000
Page 9

MARKED UP VERSION TO SHOW CHANGES MADE

In the claims:

Claim 1 has been amended as follows:

1. (four times amended) A microencapsulated and enteric coated composition comprising:

a) a microencapsulated and enteric coated mixture of sorbents with specific adsorption affinities for uremic toxins wherein the sorbents comprises oxystarch, locust bean gum, and activated charcoal, wherein the enteric coating disintegrates and dissolves at or above a PH of 7.5; and

b) a bacterial source which metabolizes urea and ammonia, said bacterial source being kept within the microencapsulated coating to prevent microbial infection of patients.